

FILE 'REGISTRY' ENTERED AT 11:30:36 ON 05 APR 2001

L1 0 S POLYHEXAMETHYLENEBIGUANIDE/CN  
L2 0 S POLY HEXAMETHYLENEBIGUANIDE/CN  
L3 0 S HEXAMETHYLENEBIGUANIDE/CN  
L4 0 S HEXAMETHYLENEBIGUANIDE/CN  
L5 0 S METHYLENE BIS DIGLYCIDYL ANILINE/CN  
L6 0 S METHYLENE (3W) DIGLYCIDYL ANILINE/CN  
L7 0 S METHYLENE AND DIGLYCIDYL ANILINE/CN  
L8 1 S DIGLYCIDYL ANILINE/CN  
L9 0 S SURFACINE/CN

FILE 'USPATFULL, CAPLUS' ENTERED AT 11:44:48 ON 05 APR 2001

L10 156 S (POLY HEXAMETHYLENEBIGUANIDE) OR (POLY HEXAMETHYLENE  
BIGUANID  
L11 9 S (METHYLENE (5W) DIGLYCIDYL ANILINE) OR (METHYLENE  
DIGLYCIDYL AN

L12 ANSWER 1 OF 3 USPATFULL  
AN 2001:14440 USPATFULL  
TI Disinfectant composition providing sustained residual biocidal action  
IN Sawan, Samuel P., Tyngsboro, MA, United States  
Subramanyam, Sundar, Stoneham, MA, United States  
Yurkovetskiy, Alexander, Acton, MA, United States  
PA Surfacine Development Company, LLC, Tyngsboro, MA, United States (U.S. corporation)  
PI US 6180584 20010130  
AI US 1999-248861 19990211 (9)  
PRAI US 1999-74456 19990212 (60)  
DT Utility  
LN.CNT 1234  
INCL INCLM: 510/382.000  
INCLS: 510/131.000; 510/214.000; 510/238.000; 510/383.000; 510/385.000;  
510/386.000; 510/390.000; 510/499.000  
NCL NCLM: 510/382.000  
NCLS: 510/131.000; 510/214.000; 510/238.000; 510/383.000; 510/385.000;  
510/386.000; 510/390.000; 510/499.000  
IC [7]  
ICM: C11D003-48  
ICS: C11D003-12; C11D003-30  
EXF 510/130; 510/131; 510/140; 510/157; 510/214; 510/238; 510/382; 510/383;  
510/385; 510/386; 510/390; 510/405; 510/406; 510/412; 510/414; 510/426;  
510/427; 510/499  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 2 OF 3 USPATFULL  
AN 2000:24306 USPATFULL  
TI Non-leaching antimicrobial films  
IN Sawan, Samuel P., Tyngsboro, MA, United States  
Subramanyam, Sundar, Stoneham, MA, United States  
Yurkovetskiy, Alexander, Acton, MA, United States  
PA BioPolymerix and Surfacine Development Company, Tewksbury, MA, United States (U.S. corporation)  
PI US 6030632 20000229  
AI US 1998-151866 19980911 (9)  
RLI Division of Ser. No. US 663269  
DT Utility  
LN.CNT 1840  
INCL INCLM: 424/405.000  
INCLS: 424/409.000; 424/421.000; 424/618.000; 514/635.000  
NCL NCLM: 424/405.000  
NCLS: 424/409.000; 424/421.000; 424/618.000; 514/635.000  
IC [7]  
ICM: A01N025-08  
EXF 424/406; 424/405; 424/408-409; 424/411; 424/412; 424/421; 424/78.09;  
424/78.12; 424/78.27; 424/78.34; 424/78.35; 424/617; 424/618; 424/630;  
424/639; 424/641; 424/646; 424/649-685; 514/492-505; 514/634; 514/635;  
523/122  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 3 OF 3 USPATFULL  
AN 1999:18745 USPATFULL  
TI Antimicrobial liquid compositions and methods for using them  
IN Sawan, Samuel P., Tyngsboro, MA, United States  
Shalon, Tadmor, Brentwood, MI, United States  
Subramanyam, Sundar, Stoneham, MA, United States  
Yurkovetskiy, Alexander, Acton, MA, United States  
PA Biopolymerix, Inc, Farnham, United Kingdom (non-U.S. corporation)

Surfacine Development Company, Inc., Tyngsboro, MA, United States (U.S. corporation)

PI US 5869073 19990209  
WO 9517152 19950729

AI US 1996-663269 19961213 (8)  
WO 1994-US14636 19941219  
19961213 PCT 371 date  
19961213 PCT 102(e) date

RLI Continuation-in-part of Ser. No. US 1994-220821, filed on 31 Mar 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-170510, filed on 20 Dec 1993, now patented, Pat. No. US 5490938

DT Utility

LN.CNT 1787

INCL INCLM: 424/406.000  
INCLS: 424/404.000; 424/407.000; 424/078.340; 424/078.350; 424/617.000;  
424/618.000; 514/634.000; 514/635.000; 523/122.000

NCL NCLM: 424/406.000  
NCLS: 424/078.340; 424/078.350; 424/404.000; 424/407.000; 424/617.000;  
424/618.000; 514/634.000; 514/635.000; 523/122.000

IC [6]  
ICM: A01N025-32

EXF 424/404-406; 424/411-415; 424/422; 424/446-449; 424/486; 424/78.09;  
424/78.12; 424/78.27; 424/78.34; 424/78.35; 424/617; 424/618; 424/630;  
424/639; 424/641; 424/644; 424/646; 424/649-655; 424/409; 424/417;  
514/492-505; 514/634; 514/635; 523/122; 623/1-4; 623/7; 623/9-11

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 1 OF 3 USPATFULL

SUMM . . . In a currently preferred embodiment, the organic material comprises an adduct of polyhexamethylene biguanide polymer and an epoxide, such as **methylene-bis-N,N-diglycidylaniline**, bisphenol-A-epichlorohydrin or N-N-diglycidyl-oxyaniline.

SUMM . . . substrate. In a currently preferred embodiment, the organic matrix is formed by first reacting polyhexamethylenebiguanide with an epoxy, such as **methylene-bis-N,N-diglycidylaniline**, to form an adduct. Stable coating solutions of the resulting adduct have been obtained in both absolute ethanol and in . . .

DETD . . . and organic multifunctional epoxides. In a currently preferred embodiment, a polyhexamethylene biguanide polymer is reacted with an epoxide, such as **methylene-bis-N,N-diglycidylaniline**. The degree of hydrophobicity of the resulting adduct can be adjusted by choice of the hydrophobic agent. The organic material. . .

DETD In a currently preferred embodiment, the polymeric material is polyhexamethylene biguanide, (PHMB) and the hydrophobic agent is **methylene-bis-N,N-diglycidylaniline** (MBDGA). The preferred silver salt is a silver halide, most preferably, silver iodide or silver nitrate, which is readily converted. . .

DETD . . . (20 wt % aqueous solution sold as Cosmocil CQ by Zeneca Biocides, Wilmington, Del.), a solution containing 20 g of **methylene-bis-N,N-diglycidylaniline** (MBDGA) (Ciba Resins, Hawthorne, N.J.) dissolved in 100 mL N,N-dimethylformamide (DMF) and 130 mL ethanol, was added dropwise. The reaction. . .

DETD 1. Preparation of **Poly(hexamethylene biguanide)** (PHMB)-Epoxide (Ep) resin

DETD 1. Preparation of **Poly(hexamethylene biguanide)** (PHMB)-Epoxide (Ep) resin.

DETD 1. Preparation of spray concentrate involving **Poly(hexamethylene biguanide)** (PHMB).

CLM What is claimed is:

disinfectant composition of claim 12 wherein the water-insoluble organic compound is an epoxide compound selected from the group consisting of **methylene-bis-N,N-diglycidylaniline**, bisphenol-A-epichlorohydrin and N,N-diglycidyl-4-glycidyloxyaniline.

L12 ANSWER 2 OF 3 USPATFULL

DETD . . . mL of a 5% (weight/volume) PHMB solution in anhydrous ethanol was added to 2 mL of 5% (weight/volume) solution of 4,4'-**methylene-bis(N,N-diglycidylaniline)** (Aldrich Chemical Company, Milwaukee, Wis.) dissolved in a 4:1 (vol/vol) ethanol/acetonitrile mixture. The solution was stirred at room temperature for. . .

DETD . . . mL of a 5% (weight/volume) PHMB solution in anhydrous ethanol was added to 2 mL of 5% (weight/volume) solution of 4,4'-**methylene-bis(N,N-diglycidylaniline)** (Aldrich Chemical Company, Milwaukee, Wis.) dissolved in a 4:1 (vol/vol) ethanol/acetonitrile mixture. The solution was refluxed at 90-95 degree.

C. for. . .

DETD . . . mL of a 5% (weight/volume) PHMB solution in anhydrous ethanol was added to 2 mL of 5% (weight/volume) solution of 4,4'-**methylene-bis(N,N-diglycidylaniline)** (Aldrich Chemical Company, Milwaukee, Wis.) dissolved in a 4:1 (vol/vol)

ethanol/acetonitrile mixture. The solution was refluxed at 90-95.degree.

C. for. . .

DETD . . . mL of a 5% (weight/volume) PHMB solution in anhydrous ethanol was added to 2 mL of 5% (weight/volume) solution of 4,4'-**methylene-bis(N,N-diglycidylaniline)** (Aldrich Chemical Company, Milwaukee, Wis.) dissolved in a 4:1 (vol/vol) ethanol/acetonitrile mixture. The solution was refluxed at 90-95.degree.

C. for. . .

DETD . . . . . free

Uncoated: No coating, control

Silver coated: Coated with metallic silver

Silver + Additional coating:

.sup.1) Benzalkonium chloride thiol

.sup.2) **poly(hexamethylenebiguanide)** thiol

.sup.3) chainextended **poly(hexamethylene biguanide)**

) thiol

.sup.4) Silver halide + **poly(hexamethylenebiguanide)** overcoat

.sup.5) Silver iodide + **poly(hexamethylenebiguanide)** coating solution

.sup.6) **Poly(hexamethylenebiguanide)** coating followed by AgI/KI

introduction

Silver salt: Inorganic salt of silver halide salts such as chloride or bromide or mixed. . . .

L12 ANSWER 3 OF 3 USPATFULL

DETD . . . mL of a 5% (weight/volume) PHMB solution in anhydrous ethanol was added to 2 mL of 5% (weight/volume) solution of 4,4'-**methylene-bis(N,N-diglycidylaniline)** (Aldrich Chemical Company, Milwaukee, Wis.) dissolved in a 4:1 (vol/vol) ethanol/acetonitrile mixture. The solution was stirred at room temperature for. . .

DETD . . . mL of a 5% (weight/volume) PHMB solution in anhydrous ethanol was added to 2 mL of 5% (weight/volume) solution of 4,4'-**methylene-bis(N,N-diglycidylaniline)** (Aldrich Chemical Company, Milwaukee, Wis.) dissolved in a 4:1 (vol/vol) ethanol/acetonitrile mixture. The solution was refluxed at 90.degree.-95.degree. C. for. . .

DETD . . . mL of a 5% (weight/volume) PHMB solution in anhydrous ethanol was added to 2 mL of 5% (weight/volume) solution of 4,4'-**methylene-bis(N,N-diglycidylaniline)** (Aldrich Chemical Company, Milwaukee, Wis.) dissolved in a 4:1 (vol/vol) ethanol/acetonitrile mixture. The solution was refluxed at 90.degree.-95.degree. C. for. . .

DETD . . . mL of a 5% (weight/volume) PHMB solution in anhydrous ethanol was added to 2 mL of 5% (weight/volume) solution of 4,4'-**methylene-bis(N,N-diglycidylaniline)** (Aldrich Chemical Company, Milwaukee, Wis.) dissolved in a 4:1 (vol/vol) ethanol/acetonitrile mixture. The solution was refluxed at 90.degree.-95.degree. C. for. . .

DETD . . . mL of a 5% (weight/volume) PHMB solution in anhydrous ethanol was added to 2 mL of 5% (weight/volume) solution of 4,4'-**methylene-bis(N,N-diglycidylaniline)** (Aldrich Chemical Company, Milwaukee, Wis.) dissolved in a 4:1 (vol/vol) ethanol/acetonitrile mixture. The solution was refluxed at 90.degree.-95.degree. C. for. . .

DETD . . . mL of a 5% (weight/volume) PHMB solution in anhydrous ethanol was added to 2 mL of 5% (weight/volume) solution of 4,4'-**methylene-bis(N,N-diglycidylaniline)** (Aldrich Chemical Company, Milwaukee, Wis.) dissolved in a 4:1 (vol/vol) ethanol/acetonitrile mixture. The solution was refluxed at 90.degree.-95.degree. C. for. . .

DETD . . . . . free

Uncoated: No coating, control

Silver coated: Coated with metallic silver

Silver + Additional coating:

.sup.1 Benzalkonium chloride thiol

.sup.2 **poly(hexamethylenebiguanide)** thiol

.sup.3 chainextended **poly(hexamethylene biguanide)**  
) thiol

.sup.4 Silver halide + **poly(hexamethylenebiguanide)**  
overcoat

.sup.5 Silver iodide + **poly(hexamethylenebiguanide)**  
coating solution

.sup.6 **Poly(hexamethylenebiguanide)** coating followed by  
AgI/KI

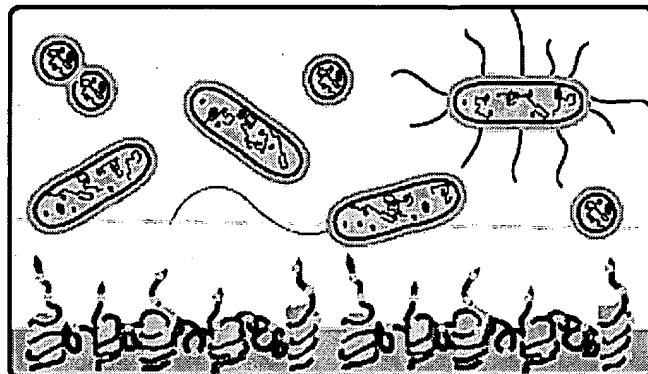
introduction

Silver salt: Inorganic salt of silver halide salts such as chloride or  
bromide or mixed.

CLM What is claimed is:

9. The liquid composition of claim 8 wherein the epoxide is 4,4'-  
**methylene-bis(N,N-diglycidylaniline)**.

# Surfacine®



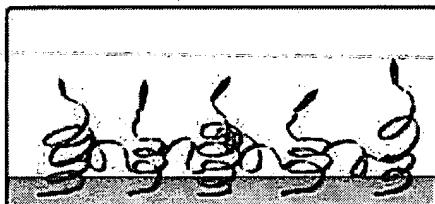
## Intelligent Antimicrobial Surfaces

Surfacine is a breakthrough silver technology. Silver has long been established as a safe and effective biocide with no human toxicity. Surfacine deploys silver in a unique way. It harnesses silver's long established safe and broad-spectrum biocidal properties and leverages them via an non-eluting, efficient delivery system that preferentially and actively transfers silver into microorganisms. This intelligent chemical delivery system differs from other silver antimicrobial technologies that deliver silver compounds non-preferentially to the microorganism's environment rather than the microorganism itself.

# Surfacine®

## Smart Polymer Technology at Work

Illustrated for medical applications. Several other formulations such as a one-part system are available.



A 3-D polymeric network is immobilized onto the substrate surface.



The immobilized surface network is impregnated with small (sub-micron) particles of silver halide that result in the formation of silver halide/polymer complex.



Solubility characteristics of the silver halide/polymeric complex prevent ionic silver from leaching into solutions contacting the surface coating.



Silver is available, however, to react with bacterial cells contacting the coating.



Silver is preferentially transferred directly to the microorganism causing a toxic accumulation that results in cell death.



Silver accumulated within dead microorganisms is not toxic to neighboring cells because it remains effectively complexed by the proteins of the dead microorganism. The silver halide reservoir within the polymeric network replenishes the coating surface with silver, allowing the coating to maintain high surface anti microbial activity to microorganisms that contact it for further challenges.

## Why silver?

Silver is a powerful antimicrobial metal and has extraordinarily low human toxicity. Silver salts, silver complexes and silver metal have played an important part in the development of medicine. Despite the fact that silver ions possess antimicrobial efficacy equal to or greater than other heavy metals ions, they have almost no toxic effects on mammals. Interest in the use of silver is being pursued in a wide variety of biomedical applications. Silver has a broad spectrum of activity (bacteria, yeast and fungi) greater than most modern antibiotics. Prior to the widespread introduction of antibiotics in the 1950's, a large number of silver-based treatments were available, some of which are still in use. Present antimicrobial use of silver includes anti-infective coatings in medical devices such as catheters, burn ointments and water purification.

The Surfacine delivery system is so efficient that the silver from a single silver dollar can be used to make over 1,000 cans of Surfacine disinfectant.



## The Surfacine Advantage

	<b>Surfacine</b>	<b>Medical Grade Disinfectant</b>	<b>Antimicrobial Agent Compounded into Bulk Polymer</b>	
<b>Mode of Application</b>	<b>Molecularly designed surface treatment</b>	Floods surface	Antimicrobial agent is compounded with polymer.	Meta depo
<b>Mode of Action</b>	<b>Surface contact only. microbial surface contact exposes organism to antimicrobial agent</b>	Chemically compromises micro-organism depending upon nature of disinfectant	Active agent diffuses to the surface where it may be leached away by contact with liquids, other surfaces, etc.	Surf as w into s
<b>Bio Availability</b>	<b>Very high for surface contact, none in solution</b>	High while immersed, none thereafter	High on fresh surfaces, low on surfaces in contact with clean solutions	High bulk
<b>Duration of Activity</b>	<b>Long term</b>	Short term. Active only while surface is wetted with agent and agent is not chemically exhausted	Depending on compatibility of active agent with polymer. Short to medium term	Long
<b>Reservoir Capacity</b>	<b>High</b>	None	Depending on compatibility of active agent with polymer. Low to high	High
<b>Leaching into Solution</b>	<b>Less than 50 ppb, often below 10 ppb</b>	Depending on the disinfectant, often 5 to 10 ppm or higher	Depending on solution contact time with surface. Often exceeds 100 ppm	Greatly
<b>Time to Kill Micro-organisms</b>	<b>Moderate</b>	Fast	Slow to moderate depending on surface concentration	Moderate
<b>Spores Activity</b>	<b>Low</b>	Moderate	Low	Low
<b>Virus Activity</b>	<b>Undetermined</b>	Depending on disinfectant	Typically none	None
<b>Toxicity to Humans</b>	<b>None</b>	High	Depending on active agent	Low
<b>Sensitivity to Surface Fouling</b>	<b>High</b>	Low	Low	Mod

<b>Vulnerability to Crevices</b>	Low	High	Low	Low
<b>Limitations</b>	Activity will be reduced with surface fouling	Must be applied repeatedly, wetting all surfaces and crevices, and remaining undiluted	Activity related to surface concentration and availability of leaching agent. Appropriate to polymeric materials	Microcontaminants
<b>Substrates</b>	Most	Most (some surfaces may be damaged by disinfectants)	Polymeric	Most
<b>Mechanical Robustness</b>	Can be engineered to meet requirements over wide range	Not applicable	Equivalent to properties of base material	Low
<b>Manufacturing Compatibility</b>	Flexible post-manufacturing process	Not part of the device	Changes material's manufacturing and mechanical properties	Vacuum
<b>Cost of disinfection activity</b>	Low for long term protection	High, assuming repeated applications	Generally low, depending on agent	High



## The Surfacine Advantage

	Surfacine	Medical Grade Disinfectant	Antimicrobial Agent Compounded Into Bulk Polymer	
Mode of Application	Molecularly designed surface treatment	Floods surface	Antimicrobial agent is compounded with polymer	Metadepo
Mode of Action	Surface contact only; microbial surface contact exposes organism to antimicrobial agent	Chemically compromises micro-organism depending upon nature of disinfectant	Active agent diffuses to the surface where it may be leached away by contact with liquids, other surfaces, etc.	Surf as w into s
Bio Availability	Very high for surface contact; none in solution	High while immersed, none thereafter	High on fresh surfaces, low on surfaces in contact with clean solutions	High bulk
Duration of Activity	Long term	Short term. Active only while surface is wetted with agent and agent is not chemically exhausted	Depending on compatibility of active agent with polymer. Short to medium term	Long
Reservoir Capacity	High	None	Depending on compatibility of active agent with polymer. Low to high	High
Leaching into Solution	Less than 50 ppb; often below 10 ppb	Depending on the disinfectant, often 5 to 10 ppm or higher	Depending on solution contact time with surface. Often exceeds 100 ppm	Greatly
Time to Kill Micro-organisms	Moderate	Fast	Slow to moderate depending on surface concentration	Moderate
Spores Activity	Low	Moderate	Low	Low
Virus Activity	Undetermined	Depending on disinfectant	Typically none	None
Toxicity to Humans	None	High	Depending on active agent	Low
Sensitivity to Surface Fouling	High	Low	Low	Moderate

Vulnerability to Crevices	Low	High	Low	Low
Limitations	Activity will be reduced with surface fouling	Must be applied repeatedly, wetting all surfaces and crevices, and remaining undiluted	Activity related to surface concentration and availability of leaching agent. Appropriate to polymeric materials	Micro contact solutes
Substrates	Most	Most (some surfaces may be damaged by disinfectants)	Polymeric	Most
Mechanical Robustness	Can be engineered to meet requirements over wide range	Not applicable	Equivalent to properties of base material	Low
Manufacturing Compatibility	Flexible post-manufacturing process	Not part of the device	Changes material's manufacturing and mechanical properties	Vacuum
Cost of disinfection activity	Low for long term protection	High, assuming repeated applications	Generally low, depending on agent	High